

Annual Reporting Form for SCEDDBO Projects and Cores

Administrative Core

Period covered by the report: 5/1/2008 – 4/30/2009

EPA Agreement Number: RD83329301-0

Investigators: Marie Lynn Miranda, Richard Auten, Sherman James, Pamela Maxson

Project Period: Year 2

Objectives of Core

The Southern Center on Environmentally-Driven Disparities in Birth Outcomes (SCEDDBO) is governed through an Administrative Core that includes an Executive Committee composed of the Director, the two Co-Directors, and the Project Manager; an Internal Steering Committee composed of members of the Executive Committee and the Directors of the Research Projects and the Facility and Community Outreach Cores; and an External Advisory Committee composed of senior environmental health scientists, as well as community representatives, with expertise relevant to SCEDDBO, who provide informal consultation, as well as annual formal evaluation of Center research and outreach activities.

The specific aims of the Administrative Core are to:

- a. Provide scientific direction and leadership;
- b. Coordinate and foster interactions among research project and facility core investigators;
- c. Provide administrative services for the Center;
- d. Direct the Young Investigators program; and
- e. Represent Duke's SCEDDBO to the university, the community, the NIH, other Children's Environmental Health Centers across the United States, and the policy and scientific community interested in children's environmental health more broadly.

In all activities, SCEDDBO emphasizes the importance of diversity. The decision to focus on health disparities, the gender and racial diversity of Center leadership, the incorporation of natural, social, and biomedical scientists, a commitment to community-based participatory research, and efforts to promote the careers of promising new investigators are all indicative of the importance that we place on fostering environments where all people can prosper.

Progress Report/Summary of Accomplishments

Quality Management Plan. The Administrative Core continued to distribute the Quality Management Plan (QMP) to all new SCEDDBO collaborators. These individuals then signed the cover sheet thereby agreeing to abide by the policies laid out in the QMP. The Administrative Core keeps a copy of these signed forms in its files. In addition, the Administrative Core performed an internal audit on the first 1000 participant datafiles for Project B: Healthy Pregnancy, Healthy Baby Study for quality assurance purposes.

Young Investigators Program. Richard Auten and Marie Lynn Miranda continue to mentor Geeta Swamy, and Sherman James (SCEDDBO's other center co-director) continues to mentor Christina Gibson-Davis.

Year two expenditures. Year two expenditures matched projections in most areas. Spending on lab costs, particularly environmental and genetic analysis, was higher than anticipated, largely due to strong enrollment and sample capture.

IRB Certification. A centralized database on IRB and IACUC certification and continuing education requirements is maintained through the Administrative Core. Twice a year, Dr. Pamela Maxson, the QA Manager, verifies that all researchers associated with SCEDDBO have completed their basic certification and continuing education requirements (one credit of continuing education is required each year to maintain certification). Reminders are sent to investigators when they are due for additional training. In addition, Dr. Maxson is responsible for ensuring IRB and IACUC Protocols are renewed and updated as necessary. All of these documents are posted to the SCEDDBO internal website, and paper copies are centrally maintained by Dr. Maxson.

Meetings. The Executive Committee meets monthly. These meetings are typically scheduled in advance of the Internal Steering Committee meetings in order to set the agenda for the larger group monthly all-hands meetings. We held two SCEDDBO retreats, one in June 2008 and one in January 2009. Retreats focused on identifying and deepening synergies across the three core projects, as well as ways to continually improve our productivity.

Website. The Administrative Core provided material on SCEDDBO to the EPA for uploading to the EPA children's centers website. In addition, we established a site describing SCEDDBO. This site is linked off the website for the Children's Environmental Health Initiative (www.nicholas.duke.edu/cehi). We also established a secure internal website that allows for discussion boards, email communication, and document storage associated with the work of each of the SCEDDBO components.

Dissemination. SCEDDBO offered a well-attended mini-symposium at the EPA in the Research Triangle Park in January 2009. This symposium was designed to present EPA employees with a synopsis of the work that SCEDDBO does, emphasizing the environmental contributors to disparities in birth outcomes. This was an excellent opportunity for discussion and feedback.

Dr. Miranda also represented the scientific mission of SCEDDBO as part of the USEPA's BOSC review of the agency's human health research program in January 2009. Specifically, Dr. Miranda co-authored and presented with Ms. Devon Payne Sturges (USEPA) a poster regarding Long Term Goal 3 entitled "Differential Vulnerability to Environmental Contaminants and Adverse Outcomes during Early Childhood." This poster was well-received and SCEDDBO was commented on very favorably by the BOSC review panel in its written report.

Dr. Miranda also brought her perspective on geospatial analysis and its usefulness in assessing and analyzing public health issues via her participation in the US Centers for Disease Control and Prevention's Geospatial Science and Healthy Communities Expert Panel, held in Atlanta, GA, in May 2008.

Training opportunities. We provided multiple training opportunities to SCEDDBO investigators and research staff. These opportunities included both intensive short course and semester long coursework for several research staff, as well as travel to professional meetings for the graduate students and post-doctoral associates supported on the SCEDDBO grant. In addition, Dr. Alan Gelfand, Director of the GISSA Core, delivered a two-day intensive short course on spatial statistics that was widely attended by SCEDDBO investigators and research staff.

New Collaborations. As part of our mission to both support the work of young investigators and advance the research mission of SCEDDBO, we began new collaborations with Dr. Staci Bilbo, Assistant Professor, Department of Psychology and Neuroscience, Duke University and Dr. Rebecca Fry, Assistant Professor, Gillings Global School of Public Health, UNC. We are

working with Dr. Bilbo on new mouse models to explore the joint impact of environmental and social stressors on birth and developmental outcomes. We are working with Dr. Fry to explore gene expression and epigenetic changes associated with *in utero* metals exposures, with a particular emphasis on cadmium. In both cases, we are working with these new investigators to develop grant applications for submission to NIH and the EPA. In addition, we established a CDC-funded collaboration with Dr. Heather Stapleton, Assistant Professor, Nicholas School of the Environment, Duke University. This study leverages our ongoing clinical obstetrics project to assess *in utero* exposures to brominated flame retardants, as well as the relationship between brominated flame retardant body burden and maternal thyroid function.

Research Project A: Mapping Disparities in Birth Outcomes

Period covered by the report: 5/1/2008 – 4/30/2009

EPA Agreement Number: RD83329301-0

Investigators: Marie Lynn Miranda (PI), Alan Gelfand, Sherman James, Pamela Maxson, Geeta Swamy

Project Period: Year 2

Objectives of Research

Project A utilizes the conceptual framework of the “weathering hypothesis,” which posits that chronic and persistent stressors lead to accelerated biological aging of women, which in turn accounts for adverse birth outcomes among certain subpopulations. The central objective is to determine whether and to what extent joint exposures to socioeconomic and environmental stressors contribute to racial and ethnic health disparities in fetal growth restriction.

Using a geographically-based nested study design moving from analysis of births for the entire State of North Carolina to six demographically and geographically distinct counties to a single health center and state-of-the-art Geographic Information Systems applications with Bayesian spatial hierarchical modeling and other advanced spatial statistical approaches, the specific aims are to:

1. Spatially link detailed birth record, fetal death certificates, socioeconomic, environmental, tax assessor, community-based, and clinical obstetric data at highly resolved scales for the State of North Carolina from 1990-2003;
2. Refine the concept of fetal growth restriction by a) developing a joint distribution for birthweight and gestation using bivariate modeling for live births and fetal deaths – both separately and jointly, and b) defining it in terms of fetal and infant mortality, rather than percentile cut points; and
3. Determine whether and to what extent differential exposures to both environmental and social stressors help explain health disparities in fetal growth restriction among a) African-American women compared to Non-Hispanic white and Hispanic women, b) Older African-American women compared to younger African-American women, c) Hispanic women compared to Non-Hispanic white and African-American women, and d) Foreign born Hispanic women compared to US born Hispanic women.

This project evaluates a large number of factors in diverse populations, providing broad relevance for birth outcomes across time, space, and demography. Identifying social and environmental factors contributing to fetal growth restriction will improve our understanding of disease etiology and explain the racial disparity in disease incidence, leading to effective interventions against poor outcomes in all population groups.

Progress Report/Summary of Accomplishments

Over the past year, the Project A research team has met both at full group level and in small groups to discuss new research ideas, review progress of current analysis and identify next steps, and work on manuscript preparation.

We have completed considerable methodological work on expected performance accruing to *synthesizing categorical datasets* with the objective of enhancing inference. We are particularly interested in how to deal with a collection of datasets of varying sizes that are all relevant to a particular scientific question, but which include different subsets of the relevant variables, with some overlap. This work attempts to synthesize cross-classified categorical datasets drawn from a common population where many of the sets are incomplete (i.e., one or more of the classification variables is unobserved), but at least one is completely observed. This is expected to reduce uncertainty about the cell probabilities in the associated multi-way contingency table as well as for derived quantities such as relative risks and odds ratios. We have made substantial progress on the underlying modeling and have developed a simulation example as well. We have also addressed the issue of the complete dataset not being a random sample from the population, as would be typical in practice. A manuscript on this work is presently in submission.

Out of efforts to develop new spatial methodologies for addressing health disparities, additional methodological work on *disaggregated spatial modeling for areal unit categorical data* is currently underway. This work uses innovative statistical methodology that extends spatial disease mapping techniques to model subgroups within areal units using a spatially smoothed, multilevel loglinear model. This work is forthcoming in the *Journal of the Royal Statistical Society, Series C*. We are also exploring the public health applications of this methodology to elucidate health disparities across space and subgroups.

We have spent considerable time linking the detailed birth record data to USEPA PM₁₀, PM_{2.5}, and ozone monitoring data in order to study the impact of *maternal exposure to air pollution* on birthweight. We are especially focused on refining exposure metrics to most effectively characterize meaningful exposures, as well as to capture any windows of vulnerability. Significant progress has been made on the relationship between birth outcomes and exposure to particulate matter and ozone separately, and the current focus is determining how to characterize joint exposure to both particulate matter and ozone. A manuscript on this work is currently in submission.

Related work has studied the use of a PM_{2.5} exposure simulator to explain birthweight. In a recently submitted paper, a template is developed for using an *environmental dose simulator* to connect ambient exposure to personal exposure. Then, using various exposure metrics, calculated from these personal exposures that are clinically plausible over the course of a pregnancy, linkage is built to adverse birth outcomes.

Our project on *racial residential segregation* has now seen the near completion of one paper (currently in preparation) which enables quantification of racial exposure/isolation at finer spatial scales within SMSA's. Such a measure can be connected to measures of social and economic disadvantage at these scales to gain insight into how racial residential segregation has manifested itself across urban landscapes. In turn, this promises to reveal key insights into how to think about the spatial aspects of the social factors influencing health disparities. We are working to determine which facets of segregation best characterize the way community-level racial residential segregation acts to promote health disparities in birth outcomes. Although our initial efforts were statewide, we have since decided that, given the significantly more detailed data available for Durham County, we will focus on this area while we work to determine what variables are most important to characterizing racial residential segregation in terms of its health consequences.

Recent work has focused on building *spatial downscalers*. Such modeling strategies enable the fusion of monitoring station data with computer model output to better assess environmental exposure at point level spatial resolution. Such downscalers can be dynamic, enabling the tracking of exposure through time. With improved estimation of local exposure, we can better examine linkage between exposure and adverse birth outcomes. A first paper on this methodology is forthcoming. Current work is developing extensions to fusion for exposure to multiple contaminants as well as to account for modeling error in the computer model output. Another recently completed manuscript (currently in submission) builds *joint models for birthweight and gestational age* using bivariate normal mixtures. Such joint modeling adjusts for maternal risk factors and provides mixture analysis of the residuals to help illuminate further subpopulations with differential risk for adverse joint birth outcomes. Modeling of the mixture components is done through gestational age and then birthweight given gestational age. Joint modeling eliminates potential causal inference concerns.

We have also submitted a review article on social and environmental contributors to disparities in birth outcomes based on both national and North Carolina data, as a way of compiling the many literatures we have accessed throughout our work on Project A.

In addition, we have been working on specific analysis and manuscripts examining the impact of maternal age and birth order on birth weight (manuscript in submission), on modeling ordinal categorical data using Gaussian processes (manuscript in preparation), and the etiology of racial disparities in maternal hypertensive disorders (manuscript in submission). We have also developed new spatial data layers on road intensity and measures of the built environment for use in upcoming analyses.

Collaborations with other SCEDDBO Components

We have worked closely with the Project C investigators to design analysis looking at the same pollutants at comparative levels of exposure from different methodological perspectives. Our discussions with the investigators of Project C help inform our methods for framing ozone and particulate matter exposures in our models, as well as help refine the planning and implementation of future animal models in Project C. In addition, we regularly trade insights with Project B regarding appropriate ways to model the joint impact of social and environmental stressors on pregnancy outcomes. In particular, as the dataset being collected under Project B reaches a size and completeness suitable for analysis, we plan to bring some of the methodological strategies developed under Project A to this dataset including synthesis with the Detailed Birth Record data, the mixture modeling for birthweight and gestational age, and the refined environmental exposure approaches.

Future Activities

We plan to continue working on each of the areas described in the progress report/summary of accomplishments section. Achieving a better understanding of exposure to air toxins, as well as particulate matter and ozone, is a central focus of our future efforts. Areas of investigation will include space time analysis of trends in births across North Carolina, an investigation of linked births (same mother) using suitable random effects models, and a more thorough investigation of the impact of introducing spatial random effects in regression modeling to explain birth outcomes.

We recently began the process of linking participants in Project B with their associated birth certificate record. We are excited to begin exploring the additional insights into the detailed birth record data that can be gleaned by linking these data with the rich dataset collected in Project B. This linkage will not only allow us to explore issues of data accuracy in the detailed birth

record, but will also allow us to begin implementing the methods of synthesizing categorical data discussed above.

We continue to target various professional audiences for dissemination of our work. Recent presentations have been at conferences under the auspices of the Joint Statistical Meetings, the American Public Health Association, the Society of Epidemiological Research, the International Biometric Society, and the Society of Maternal and Fetal Medicine.

Publications

Miranda, ML, Maxson, P, Kim DK. Early Childhood Lead Exposure and Exceptionality Designations for Students. Forthcoming, *International Journal of Child and Adolescent Health*.

Tassone, E, Miranda, ML, Gelfand, A. Disaggregated Spatial modeling for Areal Unit Categorical Data. Forthcoming, *Journal of the Royal Statistical Society*.

Berrocal, V, Gelfand, A, Holland, D. A Spatio-temporal Downscaler for Output from Numerical Models. Forthcoming, *Journal of Agricultural Biological and Environmental Sciences*.

Berrocal, V, Miranda, ML, Gelfand, A, Bhattacharya, S. Synthesizing Categorical Data to Enhance Inference. In submission.

Berrocal, V, Gelfand, A, Holland, D. Joint Data Assimilation for Ozone and PM 2.5 – a Bivariate Space-Time Downscaler under Misalignment. In submission.

Berrocal, V, Burke, JM, Gelfand, A, Holland, D, and Miranda, ML. On the use of a PM_{2.5} simulator to explain birthweight. In submission.

Anthopolos, R, Gelfand, A, James, S, Miranda, ML. A Neighborhood Level Spatial Measure of Racial Residential Isolation for Health Disparities Research. In preparation.

Swamy, GK, Edwards, S, Gelfand, A, James, SA, Miranda ML. Maternal Age, Birth Order, and Race: Differential Effects on Birthweight. In submission.

Miranda, ML, Maxson, P, Edwards, S, Swamy, GK, Gelfand, A, James, SA. Disparities in Maternal Hypertension and Pregnancy Outcomes: Evidence from North Carolina, 1994-2003. In submission.

Gray, S, Edwards, S, and Miranda, ML. Assessing exposure metrics for PM and birthweight models. In submission.

Schwartz, SL, Gelfand, A, and Miranda, ML. Joint distribution of birthweight and gestational age using mixture models. In submission.

Miranda, ML, Maxson, P, Edwards, S. Social, Environmental, and Host Factor Contributions to Disparities in Pregnancy Outcomes. In submission.

Presentations

Gray, S, Gelfand, A, Miranda, ML. Spatial Modeling of Air Pollution Exposure, Measurement Error and Adverse Birth Outcomes. Paper presentation at Eastern North American Region, San Antonio, TX, March 2009.

Gray, S, Gelfand, A, Miranda, ML. Hierarchical Spatial Modeling of Air Pollution Exposure and Measurement Error. Paper presentation at the Joint Statistical Meetings, Denver, CO, August 2008.

Berrocal, V, Gelfand, A, Holland, D. A Spatio-temporal Downscaler for Output from Numerical Models. Paper presentation at the Joint Statistical Meetings, Denver, CO, August 2008

Berrocal, V, Miranda, ML, Gelfand, A, Bhattacharya, S. Synthesizing Categorical Data to Enhance Inference. Poster presentation at Eastern North American Region, San Antonio, TX, March 2009.

Schwartz, SL, Miranda, ML, Gelfand, A. Joint Modeling of Birthweight and Gestational Age. Paper presentation at the Joint Statistical Meetings, Denver, CO, August 2008.

Miranda, ML, Maxson, P, Edwards, S, Swamy, GK, Gelfand, A, James, SA. Disparities in Maternal Hypertension and Pregnancy Outcomes. Paper presentation at the Society for Epidemiologic Research, Chicago, IL, June 2008.

Supplemental Keywords

Data fusion, meta analysis, disparities, spatial disaggregation, spatial interpolation, spatial modeling, racial residential segregation

Research Project B: Healthy Pregnancy, Healthy Baby: Studying Racial Disparities in Birth Outcomes

Period covered by the report: 5/1/2008 – 4/30/2009

EPA Agreement Number: RD83329301-0

Investigators: Redford Williams (PI), Allison Ashley-Koch, Richard Auten, Christina Gibson-Davis, Pamela Maxson, Marie Lynn Miranda, Jerome Reiter, Geeta K. Swamy,

Project Period: Year 2

Objectives of Research

The central objective of the Healthy Pregnancy, Healthy Baby Study is to determine how the interaction of environmental, social, and host factors contributes to disparities in birth outcomes between African-American and white women in the American South. There are four specific aims:

1. Conduct a cohort study of pregnant women in Durham, NC designed to correlate birth weight, gestation, and birth weight x gestation with environmental, social, and host factors;
2. Develop community-level measures of environmental and social factors by inventorying neighborhood quality and the built environment in partnership with local community groups;
3. Create a comprehensive data architecture, spatially resolved at the tax parcel level, of environmental, social, and host factors affecting pregnant women by linking data from the cohort study and neighborhood assessments with additional environmental and socioeconomic data; and
4. Determine whether and to what extent differential exposures explain health disparities in birth outcomes by applying innovative spatial and genetic statistical methods to:
 - a. Identify environmental, social, and host factors that cluster to predict birth outcomes in the entire sample,
 - b. Determine whether these clusters are more or less present in African-American versus white populations and quantify the proportion of health disparities explained by differences in cluster frequency, and
 - c. Identify environmental, social, and host factors that cluster to predict birth outcomes within the African-American and white sub-samples and compare these clusters across racial groups.

Progress Report/Summary of Accomplishments

As of 4/30/09, 1390 women have been enrolled in the study, with only 128 women withdrawn or lost to follow-up. Women are recruited from Duke University Medical Center (DUMC) and Lincoln Community Health Center. Demographic data indicate that we are successfully recruiting women who are most at risk for adverse pregnancy outcomes, particularly low-income, low educational attainment, and non-Hispanic black women.

The following information is collected from participants in the Healthy Pregnancy, Healthy Baby Study:

- Psychosocial measures include: CES-D, perceived stress, self-efficacy, interpersonal support, paternal support, perceived racism, perceived community standing, pregnancy intention, John Henryism Active Coping Scale, NEO Five Factor Inventory of personality.
- Environmental exposure survey measures include: short survey on fish consumption, smoking pattern and exposure to second-hand smoke, and drinking water source.

- Maternal and neonatal medical record abstraction includes: detailed pre-pregnancy medical and social history, antepartum complications, birth outcomes, and neonatal complications.
- Blood samples for genetic and environmental analysis to assess candidate genes related to environmental contaminant (nicotine, cotinine, cadmium, lead, mercury, arsenic, and manganese) metabolism, inflammation, vascular dysfunction, and stress response.
- Cord blood and placental samples are currently being stored for future genetic analysis and evaluation of activity at the maternal-fetal interface.

We have been highly successful in collection of participant-level data as well as biological samples, with greater than 90% attainment of maternal blood sample for genetic and environmental analyses. Collection of cord blood and placental samples, which began in June 2007, has also been successful with approximately 485 delivery samples collected.

All maternal data is georeferenced (i.e., linked to the physical address of the mother) using Geographic Information System (GIS) software. The Healthy Pregnancy/Health Baby Study also includes an in-depth neighborhood assessment designed to capture both built environment and community-level social stressors and community resources. The cohort study and neighborhood assessment data are spatially linked to extensive environmental and demographic data at a highly resolved spatial scale.

To date, we have generated genotypes on approximately 1000 blood samples from pregnant women for 104 Single Nucleotide Polymorphisms (SNPs) in sixteen genes. Candidate genes include those involving human environmental contaminant clearance (heavy metals and environmental tobacco smoke), infection and inflammation (cytokines, chemokines, and bacterial pathogen recognition), maternal stress response (serotonin), and other pathways that have been implicated as potential drivers of health disparities (vascular responsivity). Genotyping will continue in year 3, as our currently proposed candidate list includes approximately 50 different genes.

Statistical analysis regarding candidate gene polymorphisms began in June 2008 and is ongoing. Preliminary genetic analyses are described below.

The ***Vitamin D receptor gene (VDR)*** has a wide variety of functions, including calcium homeostasis and modulating circulating levels. Subtle genetic variation has also been linked to adverse conditions including diabetes, cancer, renal disease, and autoimmune disorders. In multivariable regression modeling, we found a significant association between the VDR variant (rs731236, a coding, synonymous SNP) and preterm birth ($p=0.04$) for non-Hispanic black (NHB) women in our study population. The odds of having an infant born preterm were 2.9 times higher for women with the CC genotype at this marker compared with women with the TT genotype ($p=0.04$) and were 3.8 times higher for women with the CC genotype compared with women with the CT genotype ($p=0.01$). This same association did not hold true among the non-Hispanic white (NHW) women. Furthermore, in addition to 6 other SNPs within the VDR gene, rs731236 was also associated with infant birthweight among NHB but not NHW women. Such analyses exemplify how genetic variation may contribute to racial differences in health outcomes.

The ***nitric oxide (NO) pathway*** is critical for managing oxidative damage in a variety of tissues. Reduced levels of endothelial nitric oxide synthase (NOS3) have been previously linked to pre-eclampsia, a maternal complication associated with preterm birth while specific polymorphisms within the inducible nitric oxide synthase (NOS2A) have been associated with protection against malarial infection. In adjusted multivariable regression modeling, marker rs7295972 in NOS1

was nominally associated with the occurrence of preterm birth in NHB mothers ($p=0.02$). The odds of having an infant born preterm were 2.3 times higher for women with the GG genotype at this marker compared with women with the AG genotype ($p=0.007$). The most significant association with preterm birth was observed with marker rs3918186 in NOS3 ($p=0.006$) where mothers with the AA genotype had 5.6 times greater risk for preterm infants compared with mothers with the TT genotype ($p=0.004$) and these AA mothers had 7.2 times greater risk for preterm infants compared with mothers with the AT genotype ($p=0.001$). Importantly, no nominal associations with PTB was detected with any of the SNPs in the three NOS genes within our subset of NHW mothers, consistent with a previous report which found no association of SNPs in NOS3 with pre-eclampsia within a Caucasian population. These same SNPs were examined for their association with infant birthweight. In NOS2A, the marker that had trended toward association with preterm birth (rs3794766) was very strongly associated with birthweight in the NHB mothers ($p = 0.004$). From these analyses, we conclude that maternal genotypes of genes in the NO pathway are associated with preterm birth and infant birthweight but with differential effects across racial subgroups.

Manuscripts are in preparation on both the VDR and NO pathway genetic analyses.

Ongoing statistical analysis includes genes encoding G-protein coupled receptor kinases (GRK) which have been linked to racial differences in vascular responsivity. Specifically, polymorphisms in the GRK-5 gene have demonstrated a pharmacogenomic interaction among African Americans in the setting of cardiovascular disease and response to β -adrenergic receptor (β AR) blockade, which is standard therapy for cardiac failure and ischemia.

Maternal blood samples obtained at the time of delivery are used to assess heavy metal exposures and environmental (second-hand) tobacco smoke exposure. Table 1 describes preliminary results of our environmental assays among 989 participants who have delivered their pregnancies.

Environmental Measure	All participants (N = 989)
Detectable lead	21.7%
Detectable mercury	26.9%
High mercury (pregnancy standard)	1.8%
Cadmium (>50 th percentile)	30.2%
Elevated cotinine	22.6%
Elevated manganese (CDC standard)	1.2%

Although 21.7% of study participants had detectable blood lead levels (BLL), there were significant differences by race, with 26.9% of Hispanic women having detectable levels compared to 22.1% of non-Hispanic blacks (NHB) and 14.7% of NHW. Very few women (1.8%) had elevated mercury levels compared to the CDC's pregnancy standard. However, 30% of our sample population had cadmium levels above the 50th percentile, with notable racial differences (30.4% for NHBs, 25.8% for NHWs, and 23.8% among Hispanics). Elevated cotinine levels, representing significant tobacco smoke exposure, were detected among 22.6% with racial

differences contrary to what would be expected. National estimates of smoking during pregnancy suggest that NHW women smoke more than NHB or Hispanic women (15.7% vs. 9.1% and 3.7%, respectively). However, for the women in our sample population, NHBs had a higher rate of elevated cotinine levels at 26.6% compared to 17.9% for NHWs and 9.5% for

Hispanics. Analyses are ongoing to determine what factors contribute to such race differences in environmental factors and what role they may play in gene * environment interactions.

In addition to environmental exposures, social factors can also interact with environmental exposures and maternal genes and ultimately lead to health disparities in adverse pregnancy outcomes. An extensive array of psychosocial measures is obtained from study participants through self-completed surveys. Preliminary analysis shows that although the distribution of scale summary scores across race subgroups is similar for many of the survey instruments, several psychosocial measures differ significantly by race. In our sample population, there were no apparent differences in mean raw scores for self-efficacy or perceived stress between NHB, NHW, and Hispanic women. However, both NHB and Hispanic women had more depressive symptoms than NHW women, as measured by the Center for Epidemiologic Studies Depression Scale (CES-D) scores of 15.5 and 14.5 versus 11.7, respectively ($p < 0.0001$). Furthermore, there are notable differences in personality domains across race subgroups, as measured by the NEO Five Factor Inventory (NEO-FFI). The NEO-FFI is an abridged version of the NEO-PI and gives measures of the five critical domains of adult personality: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. NHB women in our study have higher levels of neuroticism and lower levels of extroversion, openness, and agreeableness as compared to NHW women in our study. There was no difference in conscientiousness by race. High levels of neuroticism, defined as the tendency to experience negative emotions such as anxiety, anger, and depression, may plausibly be associated with adverse pregnancy outcomes such as preterm birth – an area of current analysis. Furthermore, there is some evidence to suggest that specific personality domains and facets are associated with specific genetic variants and polymorphisms. Therefore, future analyses will focus not only on how personality measures are associated with adverse pregnancy outcomes, but also how they either vary or interact with genetic differences.

Psychosocial Indicators. Preliminary analyses have been completed on psychosocial influences on birth outcomes. Pregnancy intention is an important indicator of behavior and psychological health during pregnancy. We continue to investigate the influences intention and psychosocial health have on birth outcomes. This work was presented at the UNC Women's Health Research Day as well as at a Perinatal Health Committee meeting at the NC legislature. A draft manuscript is in progress and will be ready for submission early in year 3. Additionally, work has begun examining the influences of psychosocial health and smoking status.

Collaborations with other SCEDDBO Components

Collaborative efforts with investigators from other components of SCEDDBO are ongoing. Plans for protein and candidate gene analyses are being formulated and finalized in conjunction with investigators from Project C such that associations with adverse birth outcomes as well as gene-environment interactions can be further evaluated or replicated in the mouse model system and vice versa. Analyses of psychosocial stressors in relation to birth outcomes are being devised in combination with investigators from Project A who have expertise in social epidemiology as well as racial disparities in health outcomes. Links between the North Carolina Detailed Birth Record (NCDBR) from Project A and the data from the Healthy Pregnancy/Healthy Baby study have been made and will allow validation of birth certificate data, as well as the impact of residential mobility on health outcomes. These linkages are also allowing us to consider the influence of the built environment on pregnancy outcomes via a nested dataset. We are also identifying predictors of maternal blood lead levels (BLLs) during late pregnancy by using data collected from Project B. Maternal BLLs have been shown to be highly correlated with umbilical cord BLLs at the time of delivery, which have been associated with adverse pregnancy complications as well as poor outcomes in infants and young children.

After identifying predictors of maternal BLLs from Project B, we would like to develop a predictive model of maternal BLLs which could be applied to a broader population such as the NC DBR in Project A.

Future Activities

In the upcoming year, we will continue to enroll study participants with our new target sample size of 1800 pregnant women. Based on analyses of the preliminary data, we are considering extending our target sample size to 2000 women to ensure full statistical powering for the many subgroup analyses we have planned.

We will continue analyses on approximately 1000 participants with complete pregnancy data, genetic results, and environmental results. Analyses will look at the joint impact of environmental, social, and host factors on birth outcomes, especially as they differ by and within race. Identification of such co-exposures could lead to development and implementation of strategies to prevent adverse birth outcomes, ultimately decreasing or eliminating the racial disparity.

Publications

Swamy, GK, Garrett, ME, Miranda, ML, Ashley-Koch, AE. Maternal Vitamin D Receptor Genetic Variation Contributes to Infant Birthweight among Black Mothers. In preparation.

Ashley-Koch, AE, Garrett, ME, Swamy, GK, Miranda, ML. NOS Genetic Variation Contributes to Birthweight Differentially by Race. In preparation.

Maxson, P, Miranda, ML. Pregnancy Intention and Health Disparities. In preparation.

Ingram, A, Maxson, P, Miranda, ML. Psychosocial Differences between Smokers and Non-smokers during Pregnancy. In preparation.

Zhang, X, Reiter, J. Bayesian Inference after Multiple Imputation. In preparation.

Presentations

Garrett, ME, Swamy, GK, Ellis, N, Maxson, P, Miranda, ML, Williams, RB, Ashley-Koch, AE. VDR Genetic Variation is Associated with Birthweight among African American Mothers. Poster presentation at the American Society for Human Genetics Annual Meeting, Philadelphia, PA, November 2008.

Swamy, GK, Ellis, N, Garrett, ME, Maxson, P, Miranda, ML, Williams, RB, Ashley-Koch, AE. MPO Genetic Variation is Associated with Birthweight, Particularly among African American Women. Poster presentation at the American Society for Human Genetics Annual Meeting, Philadelphia, PA, November 2008.

Ingram, A, Maxson, P, Miranda, ML. Psychosocial Differences between Smokers and Non-smokers during Pregnancy. Poster presentation at UNC Women's Health Research Day, Chapel Hill, NC, April 2009.

Maxson, P, Miranda, ML. A Multidimensional Approach to Pregnancy Intention. Poster presentation at UNC Women's Health Research Day, April 2009, Chapel Hill NC.

Maxson, P. Disparities in Pregnancy Outcomes. Invited speaker, North Carolina Perinatal Health Committee, Raleigh, NC, March 2009.

Supplemental Keywords

Pregnancy, preterm birth, low birth weight, racial disparity, African American, environmental stressors, gene-environment interactions, psychosocial stressors, genes, single nucleotide polymorphisms

Research Project C: Perinatal Environmental Exposure Disparity and Neonatal Respiratory Health

Period covered by the report: 5/1/2008 – 4/30/2009

Date of report: 7/1/2009

EPA Agreement Number: RD83329301-0

Investigators: P.I.: Richard L. Auten, Co-Inv: W. Michael Foster

Project Period: Year 2

Objectives of Research: Specific Aims

1. To determine whether maternal exposure to airborne particulates (PM) and/or ozone (1st hit) restricts fetal growth and/or postnatal growth, and impairs lung development/function in newborn mice;
2. To determine whether PM and/or ozone exposure 're-programs' maternal inflammatory responses;
3. To determine whether postnatal (2nd hit) ozone exposure further impairs postnatal somatic and lung development/function following maternal PM and/or ozone exposures;
4. To determine whether genetic or developmental susceptibility to airway hyperreactivity exacerbates maternal and/or postnatal exposure effects on postnatal somatic and lung development/function.

Progress Report/Summary of Accomplishments

1. We have submitted a manuscript (in revision) that reports the effect of prenatal diesel particulate pulmonary exposure on postnatal ozone induced airway hyperreactivity. Our report shows: dose-dependent effects of particulate matter inhalation on maternal inflammatory responses; synergistic effects of prenatal diesel exposure and postnatal ozone exposure on lung inflammatory cytokine responses, synergistic effects of prenatal diesel and postnatal ozone on postnatal airway hyperresponsiveness to inhaled methacholine challenge.
2. We have expanded these studies by using prenatal exposures to spontaneous inhalation of fresh diesel generated by internal combustion automobile engines in collaboration with Dr. Ian Gilmour, US-EPA. As with the instilled particulate matter (St. Louis particle, NIST+1648), pups born to dams exposed to environmentally relevant concentrations (2 mg/m³) of fresh diesel exhaust had worse ozone-induced airway hyperresponsiveness than those born to control-exposed dams. We found this effect was concentration dependent, with the effects of exposure to 2.0 mg/m³ more severe than exposure to 0.5 mg/m³. Importantly, the prenatal exposure to diesel exhaust combined with postnatal/perinatal ozone exposure led to persistence of airway hyperresponsiveness in adult mice even after stopping exposures for 4 weeks. These findings were presented at the 2009 Pediatric Academic Societies annual meeting in Baltimore. This implies that the perinatal exposure effects may have permanent health effects that persist to adulthood. We are trying to determine if the persistent vulnerability to increased responsiveness to methacholine challenge is attributable to altered afferent innervation, as suggested in some recent reports. So far, studies conducted in animals subjected to cervical vagotomy have not shown alterations in methacholine responsiveness, which would suggest that the altered phenotype may be due to alterations in smooth muscle

responsiveness or altered efferent signaling. A second manuscript is in preparation to describe these findings.

3. We are currently analyzing placental inflammatory mediators from fetuses carried by diesel and particulate matter exposed mice obtained at E18 (full-term: 20-21 days).
4. We have conducted preliminary studies that restrict nesting/housing resources during pregnancy as a model of non-chemical stressor exacerbations of chemically impaired perinatal toxicity. Our preliminary findings have shown that deprivation during pregnancy adds to the adverse effect of nesting restriction (housing deprivation) on postnatal weight gain during the immediate postnatal period.

Collaborations with other SCEDDBO Components

Results from Project C have been shared with project leaders, and we have accordingly refined the analysis of environmental exposure correlations with health effects markers in Project A. We are also exchanging insights with investigators from Project B on parallel results in the animal and human cohorts.

Future Activities

1. We are presently conducting studies of combined pre and postnatal air pollutant exposure (diesel, ozone) in mouse strains with genetic susceptibility to and resistance to ozone-induced airway hyperresponsiveness to determine the genetic contribution to the synergistic effects of prenatal maternal inflammation with postnatal ozone-induced airway hyperresponsiveness. Preliminary studies conducted with ozone exposed neonatal mice lacking the gene *NQO1* (NAD(P)H quinone oxidoreductase) suggest that this component of the inflammatory response cascade is important to ozone-induced airway hyperresponsiveness. These findings were presented at the 2009 annual American Thoracic Society International Conference at San Diego.

Publications

1. **Auten RL**, Mason SN, Potts EN, Fischer BM, Huang Y, Foster WM. Maternal exposure to particulate matter increases postnatal ozone-induced airway hyperreactivity in juvenile mice. In submission.

Presentations

1. **Auten RL**, Mason SN, Potts EN, Gilmour MI, Foster WM. "Maternal Diesel Exhaust Particle (DEP) Inhalation Worsens Postnatal Ozone induced Airway Hyperreactivity (AHR) in Mice" Pediatric Academic Societies, Baltimore MD, 2009.
2. Potts EN, **Auten RL**, Mason SN, Foster WM. Pulmonary susceptibility of neonatal mice to ozone modulated by NQ01. American Thoracic Society International Conference, San Diego CA, 2009
3. Visiting Pulmonary Scholar Program, "Pre-natal inhaled pollutant exposure augments postnatal ozone induced airway hyperresponsiveness" **Auten RL**. Friday Center, University of North Carolina at Chapel Hill, October 8, 2008
4. Pediatric Grand Rounds, Duke University Medical Center: **Auten RL** "Fetal and Neonatal Programming of Child and Adult Lung Diseases." August 5, 2008.

Supplemental Keywords

Airway hyperreactivity, diesel exhaust particles, air pollution, lung function

Community Outreach and Translation Core

Period covered by the report: 5/1/2008 – 4/30/2009

Date of report: 5/1/2009

EPA Agreement Number: RD83329301-0

Investigators: Martha H. Keating, Marie Lynn Miranda

Project Period: Year 2

Objectives of Research

The central objective of the Community Outreach and Translation Core (COTC) is to create, implement, and assess strategies to translate and apply the findings of the Southern Center on Environmentally-Driven Disparities in Birth Outcomes (SCEDDBO) into relevant information for women of childbearing age, families, community groups, policy makers, and health care professionals. The COTC conducts environmental health outreach and education directed at low income and minority women and their children; enhances the capacity of disadvantaged communities to understand threats posed by environmental contaminants; and provides a bridge between campus research, communities and policy makers. The specific aims of the COTC are:

1. Support the community-based neighborhood assessment being undertaken as part of Research Projects A and B;
2. Partner with nursing programs at Duke-affiliated hospitals to develop and present curricula to nursing students on environmental exposures and maternal and child health outcomes;
3. Develop culturally-appropriate advisory materials on environmental contaminants for low-income expectant or nursing mothers with low English proficiency;
4. Deliver training to local health department personnel focused on environmental factors related to maternal health and pregnancy outcomes;
5. Participate in regional, state and federal policy dialogues to provide decision makers with policy-relevant science-based information concerning environmental exposures and health disparities related to maternal and child health and well-being; and
6. Increase awareness of maternal health and health disparities by facilitating bi-directional exchanges between Center investigators, community members, public health advocacy groups, and policy makers.

Summary of Accomplishments

The goals for Year 2 of the COTC were to build on the accomplishments of Year 1 and to expand communication and translation efforts to specific audiences. A principal activity that has been accomplished in Year 2 is the development and implementation of a comprehensive communication strategy. The communication strategy has provided a consistent structure and mechanism for tracking activities and for preparing and disseminating appropriate outreach and translation materials. In addition, a new SCEDDBO website was launched off of the Children's

Environmental Health Initiative main website. Examples of different communication strategies and materials that have been used in the past year include:

- SCEDDBO website (and linked website for the Community Assessment Project),
- summary reports (overview of research findings accessible to the informed lay public),
- media contacts,
- informal information exchange with peer researchers,
- community and professional meetings and conferences, and
- peer-reviewed publications.

The communication strategy also has been successful in integrating the work of the different research projects with the activities of the COTC. Each investigator has actively contributed to COTC activities.

In addition, in Year 2, COTC personnel initiated and completed a second phase of data collection for the Community Assessment Project (CAP). This phase included expanding the study area to over 17,000 tax parcels, which includes the residential addresses of over 40% of the participants in the Healthy Pregnancy, Healthy Baby Study (Project B). This expansion will enhance data analysis for environmental stressors for SCEDDBO Project B by providing a detailed characterization of the local neighborhood environment for a significant subset of participants.

The CAP data collection team consisted of four undergraduate interns from the DukeEngage Program, a high school intern from the Josephine Dobbs Clement Early College High School at North Carolina Central University, and was led by a Masters of Environmental Management student at the Nicholas School of the Environment. From May 2008-August 2008, the team assessed the entire study area in addition to attending community meetings and processing data in CEHI's data warehouse.

For the dissemination of the results of the CAP, the COTC is targeting multiple audiences with different outreach mechanisms: publication of a descriptive report, creation of web-based resources, and in-person presentations. Presentations and visits are ongoing with a focus on CAP data and maps. These conversations take place at community meetings, as well as scheduled appointments with interested stakeholders. Since the beginning of the second phase of the project, COTC staff has attended 7 community meetings in Durham. Following the mail-out of the upcoming detailed report, COTC personnel will schedule a new series of community meetings to support the dissemination effort for this project. Beginning with the Partners Against Crime districts in Durham, COTC personnel will attend community meetings across the network of community-based organizations to discuss and display the results of the CAP and work with interested stakeholders on how to utilize the CAP results in their community development efforts.

Complementing the in-person presentations of information, the COTC has developed a detailed report of the results from the data collection: "The Community Assessment Project – Durham, North Carolina". The 20-page report, which we plan to publish in Year 3, consists of lay language explanations of the motivation behind the project, as well as the variables used in the data collection. The 15 maps in the document give it a distinct emphasis on visual presentation of the data. This report will be professionally printed and bound, and will be mailed to a targeted list of key community leaders in Durham in addition to being made publicly available on the project's new website. The CAP website (<http://cehi.env.duke.edu/cap/>) was launched this year

to provide information about the project as well as make the results available to the wider community. On the website, users will be able to download a PDF copy of the detailed report, as well as find each map used in the report available for individual download. For disseminating the data and results to stakeholders interested in exploring the results further, the COTC has developed a web-based GIS where users can interact with data layers from the CAP results, identify data attributes on demand, and create custom maps.

Specific Aim 2 of the COTC is to partner with nursing programs at Duke-affiliated hospitals to develop and present curricula to nursing students on environmental exposures and maternal and child health outcomes. Implementing activities to address this Specific Aim will be a focus of COTC efforts in Year 3. We have already designed a comprehensive project to address this aim. This proposed project consists of three linked activities: 1) integration of environmental health content into the curriculum of an Accelerated Bachelor of Science in Nursing program at Duke University through the community health nursing course; 2) development and provision of online teacher and student resources that will enable nursing faculty at any location to incorporate environmental health concepts into nursing curriculum and nursing practice; and 3) development and accreditation of an online continuing nursing education (CNE) module focused on environmental health. The resources developed during this project will provide: (1) an organized synthesis of current information; (2) foundational knowledge for nursing school faculty; and (3) subject modules on environmental health concepts that can be incorporated into existing nursing curricula. The CNE module will supply self-paced training for practicing nurses and will help fulfill annual requirements for continuing nursing education. This project has the potential for wide application because it will primarily be web-based, Boards of Nursing throughout the United States will accept the CNE accreditation, and the module format can serve as a template for numerous additional environmental health topics.

COTC staff continued collaboration with the North Carolina Preconception Health Task Force until the group concluded its mission with the development of the North Carolina Preconception Health Strategic Plan. Following this effort, COTC staff joined with the Women's Health Branch to plan a Women's Health Summit for policy makers and upper level managers representing different segments of the public health community. Unfortunately, the event was indefinitely postponed due to travel and meeting restrictions placed on state employees. If possible, this event will be held in Year 3.

Collaborations with other SCEDDBO Components

COTC staff meets monthly with the SCEDDBO investigators to keep apprised of research developments and findings, translation opportunities, and scientific outreach activities (e.g., meetings, presentations and manuscripts) of the SCEDDBO investigators. The COTC staff also provides the investigators with updates on COTC activities and opportunities to participate in outreach activities. During Year 2, as part of the communication strategy, COTC staff received a monthly update from each SCEDDBO investigator detailing any presentations, conferences, or other issues or occasions that might constitute a research translation opportunity. These regular and frequent communications enable COTC staff to keep abreast of research progress, update the website, and plan for more extended and/or extensive translation efforts.

External Collaborations

The COTC has developed a wide and diverse network of collaborators among federal, state and local agencies, universities, and community groups. Activities with these diverse partners cover

a broad spectrum of children's environmental health issues, ranging from birth outcomes to lead poisoning prevention, environmental exposures, and obesity.

COTC staff has developed working relationships with scientists at the USEPA representing a wide variety of disciplines. As part of an effort to extend these relationships, COTC staff collaborated with EPA staff to plan and present a mini-symposium for EPA scientists at the Research Triangle Park campus. During a 3-hour session, all SCEDDBO investigators gave a brief overview of their research project and results to date. A question and answer period presented the opportunity to discuss cross-cutting issues and EPA research priorities. As a result, the COTC is now frequently contacted by EPA in order to exchange ideas and research findings. These relationships have resulted in periodic meetings with EPA staff specifically related to:

- ozone and PM exposure and its relationship to birth outcomes,
- methods for using the North Carolina detailed birth record for exposure analysis,
- environmental justice issues,
- exposure near roadways, and
- community involvement and outreach.

Activities with multiple state agencies continue to cover a wide variety of topics including the impact of the built environment on obesity and pregnancy outcomes, mapping environmental exposures and built environment variables, as well as other topics related to school-aged children. The COTC is actively working with staff at numerous state offices, particularly within the Division of Public Health. These offices include: Senior Advisor for Healthy Schools, Women's Health Branch, and Nutrition Services Branch

SCEDDBO investigators again mentored a student in the "Break the Cycle" project sponsored by Region 4 of the USEPA, Emory University, and the Southeast Pediatric Environmental Health Specialty Unit. The student selected his own topic and will present his findings at the 4th Break the Cycle in September 2009.

Finally, the COTC continues to respond with detailed information to numerous requests from private citizens about a variety of environmental health concerns. These requests were received through both the CEHI toll-free number and via the CEHI website.

Future Activities

Activities planned for the COTC in Year 3 will build on the accomplishments of Years 1 and 2. We will continue to expand communication and translation efforts to specific audiences. With a communication strategy in place, the COTC will continue to utilize various communication tools appropriate to a variety of audiences. Collaboration with researchers and groups external to SCEDDBO will continue to evolve and the COTC will continue to welcome and respond to requests for environmental health information to community groups as well as the general public.

Publications

Henderson, K., Maxson, P. Obesity Intervention Strategies and the Built Environment in a Low-Income, Minority Population. *International Journal of Child and Adolescent Health*. In press.

Koehrn, K., Keating, M. The Regulation of Agricultural Pesticides in North Carolina: Implications for Farm Workers and Their Families. *International Journal of Child and Adolescent Health*. In press.

Presentations

Henderson, K., Maxson, P. Obesity Intervention Strategies and the Built Environment in a Low-Income, Minority Population. Paper Presentation, Break the Cycle III Conference, Atlanta, GA. May 2008.

Koehrn, K., Keating, M. The Regulation of Agricultural Pesticides in North Carolina: Implications for Farm Workers and Their Families. Paper Presentation, Break the Cycle III Conference, Atlanta, GA, May 2008.

Miranda, ML. Effective Interventions for Preventing Lead Poisoning. USEPA Beyond Translation Workshop, Research Triangle Park, NC, October 2008.

Southern Center on Environmentally-Driven Disparities in Birth Outcomes. Research Symposium presented at the USEPA, Research Triangle Park, NC, January 2009. (All investigators participated.)

Supplemental Keywords

Risk communication, outreach, translation, participatory research, built environment

Geographic Information System and Statistical Analysis Core

Period covered by the report: 5/1/2008 – 4/30/2009

EPA Agreement Number: RD83329301-0

Investigators: Alan Gelfand (PI), Allison Ashley-Koch, Jonathan Goodall, Marie Lynn Miranda, Jerome Reiter

Project Period: Year 1

Objectives of Research

The overall objective of the GIS and Statistical Analysis Core is to **support spatial and quantitative analysis needs of the Center research projects, as well as the Community Outreach and Translation Core.** Our specific aims include:

1. Providing support for the development of environmental and social data layers needed to implement data analyses required for the research projects and the Community Outreach and Translation Core;
2. Providing statistical analysis, advice, and consulting on the broad range of statistical issues that arise in conjunction with the research projects, with a particular emphasis on data reduction methods and modeling spatial and spatio-temporal data within a Bayesian framework; and,
3. Providing analysis for the unique needs of genetic data arising from the clinical and animal studies of the center.

This support core facilitates the development of innovative quantitative methodology for children's environmental health research associated with the projects and cores. Equally important, it will enhance substantive collaboration between statisticians and scientists involved in the research projects yielding improved analyses of research core data, as well as novel statistical modeling.

Progress Report/Summary of Accomplishments

In the second year of the project, the GISSA Core has continued to focus on developing the data warehouse providing underlying support for all other Center components. We have acquired and georeferenced additional detailed birth record data, continued genotyping blood samples from the participants in Project B, and continued providing data management support as Project B continues to enroll additional participants.

We now have in hand identified North Carolina Detailed Birth Records (DBR) at the individual subject level, giving us access to 18 years of birth data covering 1990-2007. The DBR is compiled from questionnaires obtained at the time of birth certificate filing and includes elements essential to our proposed analyses. Available variables include, *inter alia*: maternal residence and state and country of birth; marital status; maternal and paternal race, Hispanic ethnicity, and education; alcohol and tobacco use; plurality; parity; maternal complications; congenital anomalies; whether an infant death certificate was filed; and infant birth weight and gestational age. All 18 years of data have been integrated and standardized to facilitate data linkages and statistical analysis.

In addition to incorporating the most recently available North Carolina DBR data into the GISSA Core data warehouse, we have also worked to acquire additional birth data that will enhance various research projects across SCEDDBO. We have received historical NC DBR data for 1978-1989. Although this data does not contain all the detail available in more recent years, such historical data will enable us to examine trends in birth outcomes across the state. Additionally, we have initiated communication with the vital records offices of the other states in Region 4 in order to explore the acquisition of birth data in these states.

The GIS team has worked to street geocode all residential addresses in the 1990-2007 DBR data for the State of North Carolina. Street geocoding, which allows us to link births to Census data resolved at the block level, have been georeferenced for 75% of 1990-2003 birth records, with success rates increasing over time up to 82% by 1999. Preliminary street geocoding of the 2004-2007 DBR has georeferenced 70% of the birth data, with significant increase in the success rate expected as these efforts progress. Additionally, in Durham, Pitt, Orange, and Wilson Counties, we have geocoded birth data to the individual tax parcel, with an overall success rate of 94%, 68%, 92%, and 75%, respectively. Efforts to parcel geocode all birth data for Guilford and Mecklenburg Counties are ongoing.

We have expanded the environmental data layers available for use through the SCEDDBO data warehouse. These include spatial data on road intensity, criteria air pollutants from the USEPA's AQS system, water quality, environmental releases documented in the Toxics Release Inventory, and housing quality.

We have developed methods for linking the North Carolina DBR data with participant data from Project B. All participants who delivered between 2005 and 2007 have been successfully matched to their corresponding record in the DBR. This linkage will allow us to examine how accurately the administrative dataset (DBR) captures key information, as well as undertake analysis of residential mobility during pregnancy. In addition, as more years of DBR data become available, we will be able to find future births to Project B participants and examine internatal spacing and subsequent pregnancy outcomes.

To date, we have generated genotypes on 1,000 blood samples from pregnant women for 195 Single Nucleotide Polymorphisms (SNPs) in 29 genes, primarily involved in either metabolism of heavy metals or immune response. With these data now available, we have begun statistical analysis looking at environmental and genetic contributions and interactions to pregnancy outcomes. These results are discussed in the Project B report. We anticipate further genotyping and statistical analysis in the coming year.

Collaborations with other SCEDDBO Components

By its nature, the GISSA Core is highly involved in collaborations across all Center components. We are working with the investigators of Project A to determine what spatial data layers need to be developed and at what spatial scales. We are also expanding and supporting the data architecture to facilitate linkages of the data compiled by Projects B and C in order to create opportunities for synergies across projects.

Future Activities

We will continue developing and expanding the geospatial data warehouse that supports analysis among various projects. The GIS team will continue working with investigators in Projects A and B to develop a comprehensive list of environmental spatial data layers of interest, as well as a plan for prioritizing the development of this crucial dataset.

For Buncombe, Forsyth, New Hanover, Mecklenburg, and Guilford Counties, we plan to geocode all years of the detailed birth records at the tax parcel level. This effort has already been completed for several counties. This will provide us with additional geospatial resolution, and will allow us to link the data to the tax assessor databases and, especially in Durham County, to the additional environmental and demographic overlays.

We will continue analyses on approximately 1,000 Project B participants with complete pregnancy data, genetic results, and environmental results. Analyses will look at the joint impact of environmental, social, and host factors on birth outcomes, especially as they differ by and within race. Identification of such co-exposures could lead to development and implementation of strategies to prevent adverse birth outcomes, ultimately decreasing or eliminating the racial disparity. We will also generate imputed datasets based on the methodology developed by the GISSA Core, in order to handle missing data.

As Project B continues to enroll participants, maternal blood samples will be analyzed for both protein and genetic associations with adverse birth outcomes. Maternal samples collected at 24 – 28 weeks gestation will be analyzed for protein levels involving markers of inflammation, vascular dysfunction, and stress response. DNA analysis is well underway with genotyping completed for several genetic polymorphisms regarding environmental contaminant metabolism as well as inflammatory cytokines and chemokines. Genotyping will include genes involved in the maternal stress response and vascular/endothelial cell dysfunction. Statistical analysis regarding candidate gene polymorphisms has already begun and will continue through Year 3. We will continue to genotype SNPs in the candidate genes we had proposed, as well as genotyping new, pertinent genes as the literature suggests (ie GRK2/GRK5 as described by Liggett et al., 2008).

Publications

All manuscripts supported by the GISSA Core are listed under the individual research projects.

Supplemental Keywords

Data fusion, meta analysis, disparities, spatial disaggregation, spatial interpolation, spatial modeling